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# Systematic literature analysis and review of targeted preventive measures to limit healthcare-associated infections by meticillin-resistant *Staphylococcus aureus*

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Meticillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of healthcare-associated infections in Europe. Many examples have demonstrated that the spread of MRSA within healthcare settings can be reduced by targeted infection control measures. The aim of this systematic literature analysis and review was to summarise the evidence for the use of bacterial cultures for active surveillance the benefit of rapid screening tests, as well as the use of decolonisation therapies and different types of isolation measures. We included 83 studies published between 2000 and 2012. Although the studies reported good evidence supporting the role of active surveillance followed by decolonisation therapy, the effectiveness of single-room isolation was mostly shown in non-controlled studies, which should inspire further research regarding this issue. Overall, this review highlighted that when planning the implementation of preventive interventions, there is a need to consider the prevalence of MRSA, the incidence of infections, the competing effect of standard control measures (e.g. hand hygiene) and the likelihood of transmission in the respective settings of implementation.

## Background

Meticillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of healthcare-associated infections in Europe. In 2008, the European Centre for Disease Prevention and Control (ECDC) estimated that a total number of 171,200 nosocomial MRSA infections are acquired annually in the Member States of the European Union (EU), and in Iceland and Norway, resulting in 5,400 attributable excess deaths, more than 1 million excess days of hospitalisation and EUR 380 million excess in-hospital costs [1]. The burden of MRSA infections was also shown in an analysis of data on healthcare-associated infections collected prospectively from European intensive care units (ICU) between 2005 and 2008, where 1.7% of all patients developed *S. aureus* pneumonia or bloodstream infections. A mean of 35% of these infections were caused by MRSA. Moreover, the hazard ratio for mortality was 5.6-times higher (95% confidence interval (CI): 3.4–9.4) for patients with MRSA bloodstream infection than for patients without *S. aureus* bacteraemia [2].

Among the proposed methods to prevent MRSA, many (e.g. hand hygiene and transmission-based precautions) have been used for general infection control, and their effectiveness has been reviewed extensively [3,4]. However, there is an ongoing discussion about the evidence for the effectiveness of several more specific prevention methods which, nevertheless, have been included in standards for the prevention and control of MRSA in a majority of European countries [5]. Therefore, the scope of this review was to analyse systematically recent literature (published after 2000) with respect to the following questions related to MRSA prevention and control:

1. Does screening of patients before or on admission reduce the incidence of MRSA infection or transmission? How do PCR-based rapid tests for the direct detection of MRSA from screening specimens influence the incidence of MRSA colonisation or infection compared with culture-based methods?
2. Does the decolonisation of nasal MRSA or *S. aureus* carriage using mupirocin nasal ointment, alone or in combination with other agents, reduce colonisation or the development of infections?
3. Does isolation in single rooms of patients colonised or infected with MRSA prevent the spread of MRSA better than the use of transmission-based precautions (hand hygiene, gloves, aprons) alone? What is the effect of pre-emptive isolation of risk patients for MRSA carriage (until screening results are available)?

## Methods

A systematic literature analysis and review was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6]. To identify relevant publications, PubMed, EMBASE and Scopus were searched for articles published between 1 January 2000 and 31 October 2012 in English language. The search terms were: MRSA AND (prevention OR control OR prophylaxis OR preventive measures OR preventive therapy OR preventive treatment OR precaution OR screening OR active surveillance OR decolonization OR mupirocin OR surveillance culture* OR chromogenic OR PCR OR polymerase chain reaction OR rapid test OR isolation OR hygiene OR efficien* OR effective*) AND (healthcare OR hospital OR nursing home OR long-term care facilit*); the search terms were adapted for search in EMBASE: "MRSA AND decolonization", "MRSA AND isolation", "MRSA AND screening".

Titles and abstracts were screened independently by two reviewers (RK and AWF). Studies with outcomes measuring the incidence of MRSA colonisation or infection were included. Exclusion criteria were: Studies that did not report on the effects of the preventive measures on infection or transmission; studies performed in settings other than hospitals, long-term care facilities and nursing homes; case series, outbreak reports and

**Figure**

Flow diagram for the selection of studies on preventive measures against to limit healthcare-associated infections by meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=9,340)

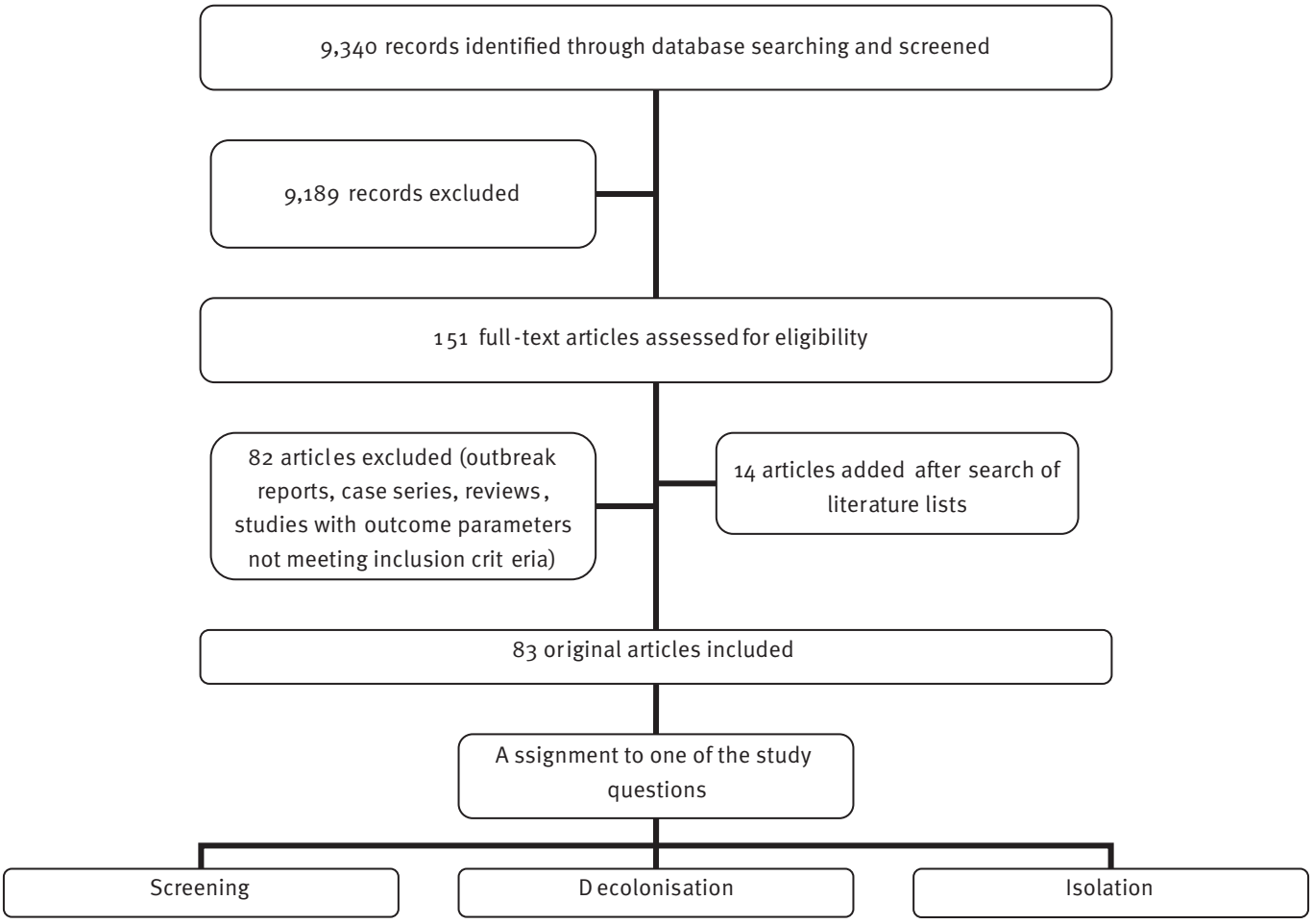

**Table 1a**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study; MRSA[a]; Time; Country; Setting; Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| Culture-based tests | | | | | |
| Camus [9]; 4.8–9%; 2002–03; France; MICU; RCT. | NA | Intervention: screening of high-risk patients (nose, perineum, wounds, aspirates) at admission, weekly thereafter and at discharge; Control: same methods as in the intervention group, but the screening results were not reported. | Gloves, gowns, mask (also pre-emptively), decolonisation | A, I | MRSA acquisition in the intervention group vs the control group: 6.5% vs 5.3%; p=0.58; Proportion of patients who acquired MRSA infection was identical: 1.6% (n=4) vs 1.6% (n=4); p>0.99; Rate of ICU-acquired infection was identical: 16.5% vs 16.5%, p=0.98. |
| Chaberny [10]; NA; 2002–06; Germany; ICU and surgery; CS (interrupted time series). | 48 h | Intervention: screening (nose, throat, wounds) of all patients; Control: selective screening of contact patients or patients with a history of MRSA carriage. | Private rooms, gowns, gloves, decolonisation | I | Change in the level of infections: -0.163 MRSA infected patients/1,000 pd (95% CI: -0.276 to -0.05); Slope: -0.01 MRSA-infected patients/1,000 pd (95% CI: 0.018–0.003). |
| Clancy [12]; 3.7%; 2003–04; United States; MSICU; CS (before-and-after). | 48 h | Intervention: nasal screening of all patients at admission and weekly thereafter; Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves | I | Decrease of MRSA infections (6.1 vs 4.1 infections/1,000 census-days; p=0.01) and of nosocomial (>72 h after admission) MRSA infections (4.5 vs 2.8 infections/1,000 census-days; p=0.01). |
| Ellingson [15]; NA; 1999–2008; United States; Hospital-wide; CS (interrupted time series). | NA | Intervention: screening (nose, wounds) of all patients at admission and at discharge + behavioural change strategies, hand hygiene, environmental disinfection; Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves | C/I | Incidence of MRSA colonisation or infection decreased by 21.8% (95% CI: 8.8–33.7) from 2.40 cases/1,000 pd to 1.88/1,000 pd at risk. |
| Eveillard [42]; 4.7–12.1%; 2003; France; Hospital-wide; CS. | NA | Intervention: screening of all patients admitted to ICUs (nose, axilla, rectal) and of high-risk patients admitted to other wards; prospective data acquisition without historical or prospective control group. | Contact precautions similar to guidelines from the United States Centers for Disease Control and Prevention | I | Incidence of MRSA from clinical specimens/100 days of hospitalisation for MRSA carriers identified at admission of was 3.1% when the programme was completely implemented, compared with 10.4% when no screening was performed (p<0.001). |
| Gould [47]; 6–16%; 1999–2003; United Kingdom; MSICU; CS (interrupted time series). | NA | Intervention: screening (nose, throat, groin, axilla) of all patients at admission; Control: phase without any or non-compulsory screening. | Private rooms, barrier-nursing (unspecified), decolonisation | C/I, B | By time series regression analysis, the proportion of patients with MRSA (infection and colonisation) decreased from 15% to 5% (95% CI: 3.5–19.3; p=0.005); no significant effect on MRSA bacteraemia rates. |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1B**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study;<br>MRSA[a];<br>Time;<br>Country;<br>Setting;<br>Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| Culture-based tests | | | | | |
| Holzmann-Pazgal [19];<br>2.7–8.3%;<br>2007–09;<br>United States;<br>PICU;<br>CS (before-and-after). | 48 h | Intervention: nasal screening of all patients at admission and weekly thereafter;<br>Control: phase without any or with non-compulsory screening. | Gloves, gowns | C/I | Yearly MRSA incidence density decreased from 2006 to 2009 (6.88 vs 1.45/1,000 pd; p<0.01);<br>and from 2007 to 2009 (7.32 vs 1.45/1,000 pd; p<0.01). |
| Lawes [38];<br>3.1%;<br>2006–10;<br>United Kingdom;<br>Hospital-wide;<br>CS without control (times series analysis). | mostly <24 h | Intervention: nasal screening of all patients at admission;<br>isolation facilities and decolonisation;<br>hand-hygiene campaign;<br>Compared to: no control group;<br>observation over time. | Private rooms, decolonisation | B | Reduction of MRSA bacteraemia (0.26/1,000 acute occupied bed days (AOBD) vs 0.07/1,000 AOBD; p<0.001). In a multivariate time-series analysis, introduction of screening resulted in reduction of MRSA bacteraemia, hospital-associated incidence density and 30-day mortality after MRSA bacteraemia (p<0.001). |
| Huang [21];<br>12%;<br>1996–2004;<br>United States;<br>MSICU;<br>CS (interrupted time series). | 48 h | Intervention: campaigns for catheter placement, hand hygiene, nasal screening of all patients at admission and weekly thereafter introduced step by step;<br>Control: phase without any or with non-compulsory screening. | Contact isolation precautions (unspecified) | B | MRSA screening was associated with a 67% decrease in the incidence density of MRSA bacteraemia in ICUs (p<0.002), a 39% decrease in non-ICUs, and a 53% decrease hospital-wide. |
| Huskins [20];<br>9.5–12.6%;<br>2005–06;<br>United States;<br>MSICU;<br>RCT. | 5.2 ± 1.4 d | Intervention: nasal screening of all patients at admission, weekly thereafter;<br>Control: control ICUs where screening was performed as in intervention ICUs but without reporting of the results. | Gloves, gowns | C/I | Incidence of events of colonisation or infection with MRSA/1,000 pd did not differ significantly between intervention and control ICUs after adjustment for the baseline incidence (40.4 vs 35.6; p=0.35). |
| Kelly [40];<br>1.13–1.63%;<br>2005–07;<br>Ireland;<br>Orthopaedic surgery;<br>CS (before-and-after). | NA | Intervention: period 1: pre-admission screening (nose, axillae, groin) of all elective orthopaedic patients;<br>period 2: separation (admission to another hospital) of trauma patients from elective patients;<br>Control: phase without any or with non-compulsory screening. | Decolonisation prior to admission | C/I | Incidence of MRSA infections declined from 0.49% in the control phase to 0.35% (p=0.108) in period 1, and to 0.23% (p=0.05) in period 2. MRSA colonisation detected rose from 1.13% (control phase) to 1.63% (period 1) and 1.59% (period 2) (p=0.002). |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1c**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study; MRSA[a]; Time; Country; Setting; Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| Culture-based tests | | | | | |
| Lucet [43]; 6.5%; 1995–2001; France; MSICU; CS. | NA | Intervention: in period 1 and 2, nasal screening of all patients at admission and weekly thereafter; Control: prospective data acquisition without control group, in period 2 promotion of hand hygiene. | Private rooms, gloves, gowns | A | Incidence of MRSA acquisition/100 exposed patients (per 1,000 pd) decreased from 7% (5.43) in period 1 to 2.8% (2.39) in period 2. Period 2 was an independent protective factor influencing the incidence of MRSA acquisition (OR vs period 1: 0.49; p<0.0001). |
| Malde [37]; 3.2–6.7%; 1996–2004; United Kingdom; Vascular surgery; CS (before-and-after). | NA | Intervention: nasal screening of all patients at admission or for elective admissions 1– 3 weeks prior to admission; Control: phase without any or with non-compulsory screening. | Decolonisation | W/SSI | MRSA wound infections among MRSA-positive elective admissions reduced from 20/36 (56%) to 15/67 (22%) (p=0.002); among MRSA-positive emergency admissions from 35/56 (63%) to 53/121 (44%) (p=0.042). Major limb amputation rates among MRSA-positive admissions reduced from 10/36 (18%) to 6/67 (9%) (p=0.026). |
| Pan [28]; NA; 1996–2001; Italy; Hospital-wide; CS (before-and-after). | NA | Intervention: nasal screening of high-risk patients on high-risk wards at admission and in different intervals thereafter. Control: phase without any or with non-compulsory screening. | Gloves, decolonisation, gowns (only for infected patients) | B | Incidence rate of MRSA bacteraemia decreased by 42% from 0.64 to 0.37/1,000 admissions (RR 0.57; 95% CI: 0.35–0.92; p=0.03). This effect was mostly due to reduction of bacteraemia cases related to central venous catheters. |
| Reilly [27]; 3.9%; 2008–09; United Kingdom; Hospital-wide; CS (before-and after). | NA | Intervention: nasal screening of all patients at admission; Control: phase without any or with non-compulsory screening. | Private rooms, other precautions unspecified, decolonisation | C/I | MRSA infections (7.5/1,000 pd) reduced significantly over the study period (p=0.0209); admission prevalence decreased from 5.5% to 3.5% (p< 0.0001). |
| Rodriguez-Bano [30]; ca 9%; 1995–2008; Spain; Hospital-wide; CS (interrupted time series). | NA | Intervention: phase 2 screening of all patients (nose and various specimens) at admission and weekly thereafter and healthcare workers; phase 3 screening of patients admitted from other facilities; Control: phase without any or with non-compulsory screening. | Private rooms, contact precautions, decolonisation | C/I | MRSA colonisation and infection rates (0.56 cases/1,000 pd; 95% CI: 0.49–0.62) decreased significantly to 0.28 cases/1,000 pd (95% CI: 0.17–0.40) in phase 2 and to 0.07/1,000 pd (95% CI 0.06–0.08) in phase 3. |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1d**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study;<br>MRSA[a];<br>Time;<br>Country;<br>Setting;<br>Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| Culture-based tests | | | | | |
| Shitrit [31];<br>1.6–5.6%;<br>2002–04;<br>Israel;<br>MSICU;<br>Geriatric ward;<br>CS (before-and-after). | NA | Intervention: screening (nose, sputum for intubated, perineum, wounds) of high-risk patients at admission and in different intervals thereafter;<br>Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves, decolonisation | B | Mean number of MRSA bacteraemia cases per month decreased from 3.6 cases to 1.8 cases after the intervention (p<0.001). |
| Souweine [46];<br>NA;<br>1994–06;<br>France;<br>MSICU;<br>CS (before-and-after). | NA | Intervention: screening (nose, rectum) of all patients at admission, weekly thereafter and at discharge;<br>Control: phase without any or with non-compulsory screening. | Gloves, gowns, decolonisation | I | Number of patients infected by MRSA (including cases of bacteraemia, pneumonia, urinary tract infection, catheter infection, wound infection) decreased from 5.2% to 1.7% (p=0.018). |
| Thompson [32];<br>8.1%;<br>1996–2008;<br>United Kingdom;<br>MSICU;<br>CS (before-and-after). | NA | Intervention: screening (nose, throat) of all patients at admission and weekly thereafter;<br>Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves, decolonisation | A, B | MRSA acquisition/1,000 bed-days decreased from 49.0 (95% CI: 34.4–63.6) to 28.3 (95% CI: 21.7– 34.9), 19.3 (95% CI: 16.3–22.3) and 11.8 (95% CI: 7.3–16.3), respectively; MRSA bacteraemia cases/1,000 bed-days decreased from 7.6 (95% CI: 4.7–10.5) to 3.7 (95% CI: 2.6–4.8) and 0.4 (95% CI: 0–2.9). |
| Tomic [45];<br>NA;<br>1998–2002;<br>Slovenia;<br>MSICU;<br>CS (before-and-after). | NA | Intervention: screening (nose, throat, wounds and devices) of high-risk patients at admission;<br>Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves, decolonisation | C/I | MRSA cases increased from 4.5 to 8.0/1,000 admissions after implementation of screening (p=0.02); the proportion of acquired MRSA cases decreased from 50% in 1999 to 6% in 2002 (p=0.001). |
| Troché [44];<br>4.2%;<br>1995–2000;<br>France;<br>ICU;<br>CS. | NA | Intervention: nasal screening of all patients at admission, weekly thereafter and at discharge; prospective data acquisition without historical or prospective control group. | (All patients in private rooms), gloves, gowns, decolonisation | A | The overall MRSA acquisition rate was 7.9 cases/1,000 pd (p=NA); it declined in the first three years after the implementation of screening but increased again, when the admission prevalence increased. |
| Wang [33];<br>17.6–26.5%;<br>2005–06;<br>Taiwan;<br>MSICU;<br>CS (before-and-after). | 3d | Intervention: screening (nares, throat/sputum, axillae, inguinal area, wounds) of all patients at admission, every 3 days thereafter and at discharge;<br>Control: as in intervention phase but results were not reported. | Private rooms, gloves, gowns | A, I | The incidence of acquiring MRSA during ICU stay did not differ significantly during intervention and control phases in two participating hospitals (9.6% vs 9.98%; p=0.94; 13.92% vs 13.52%; p=0.81). The incidence of MRSA infection did not differ either (p=0.719; p=0.932). |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1e**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study;<br>MRSA[a];<br>Time;<br>Country;<br>Setting;<br>Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| Culture-based tests | | | | | |
| Warren [34];<br>7.2–11.4%;<br>2002–04;<br>United States;<br>SICU;<br>CS (before-and-after). | 72 h | Intervention: nasal screening of all patients at admission, weekly thereafter and at discharge;<br>Control: phase without any or with non-compulsory screening. | Private rooms, gloves, gowns | A | MRSA admission prevalence increased (7.2% vs 11.4%; p=0.001); MRSA acquisition rate constant (7.0 vs 5.5 MRSA cases/1,000 pd; p=0.29). |
| Wernitz [36];<br>20.6%;<br>1999–2002;<br>Germany;<br>Hospital-wide;<br>CS (before-and-after). | NA | Intervention: screening (nose, throat, skin, devices, wounds) of high-risk groups at admission;<br>Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves, decolonisation | I | The standardised infection ratio was 0.52 (95% CI: 0.37–0.71), indicating that 48% of the expected hospital-acquired MRSA infections were prevented. |
| West [35];<br>5.3–9.7%;<br>2001–03;<br>United States;<br>Hospital-wide;<br>CS (before-and-after). | NA | Intervention: nasal MRSA screening of risk patients at admission and weekly thereafter;<br>Control: phase without any or with non-compulsory screening. | Contact isolation, gowns, gloves | I | Mean number of nosocomial MRSA infections decreased by 39% from 0.76 to 0.45/1,000 pd (p=0.05) in one, and by 21% from 0.72 to 0.57 /1,000 pd (p=0.35) in another hospital. |
| PCR-based tests | | | | | |
| Aldeyab [7];<br>6.8–7.3%;<br>2006–07;<br>United Kingdom;<br>Medical/surgical ward;<br>CS (before-and-after). | 19.3–22.7 h / 42.2–51.8 h | Intervention: phase 1: rapid test on surgical ward (nares, axillae, groin) for all patients at admission and discharge;<br>culture-based screening (nares, axillae, groin, throat) on medical ward (4 months) for all patients at admission and discharge;<br>Control: phase 2: switch of wards and tests. | Private rooms (not for all); contact precautions (unspecified) | C/I | Hospital-acquired MRSA incidence (cases of colonisation and infection) on surgical ward not reduced: 20 (phase 1) vs 22.1/1,000 bed-days (phase 2) (p=0.69); hospital-acquired MRSA incidence rate in medical ward increased in rapid test phase: 11.8 (phase 1) vs 20.3/1,000 bed-days (phase 2) (p=0.03). |
| Awad [8];<br>18%;<br>2005–08;<br>United States;<br>Hospital-wide;<br>CS (before-and-after). | NA | Intervention: multiple measures (nasal screening of all patients at admission/transfer and discharge;<br>contact isolation of MRSA infected or colonised patients, hand hygiene campaign, cultural transformation campaign;<br>Control: phase without any or with non-compulsory screening. | Contact isolation (unspecified) | A, B, I, W/SSI | MRSA transmission decreased from 5.8 to 3.0/1,000 bed-days (p=0.05); overall MRSA nosocomial infections decreased from 2.0 to 1.0/1,000 bed days (p=0.016); overall SSI decreased (p<0.05); nosocomial MRSA bloodstream infections decreased from 2.9 to 2.5/1,000 bed-days (p> 0.05). |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1f**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study;<br>MRSA[a];<br>Time;<br>Country;<br>Setting;<br>Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| PCR-based tests | | | | | |
| Chowers [11];<br>2.7–3.7%;<br>2003–08;<br>Israel;<br>Hospital-wide;<br>CS (interrupted time series). | 24 h / 2–4 d | Intervention:<br>period 1: high-risk patients screened at admission (sample unspecified) + compliance monitoring;<br>period 2: compliance monitoring with screening/ contact isolation discontinued;<br>period 3: PCR-based screening of high-risk patients introduced (sample unspecified);<br>period 4: monitoring re-introduced and decolonisation discontinued;<br>Control: period 0 without any or with non-compulsory screening (screening of contact patients only). | Contact isolation (unspecified), decolonisation | B | Period 0 vs period 1: average number of bacteraemia cases per 1,000 pd was reduced by factor 0.55 (95% CI: 0.36–0.83); period 0 vs period 4: average number of bacteraemia cases per 1,000 pd decreased by a factor of 0.27 (95% CI: 0.14–0.58); period 1 vs period 4: average number of bacteraemia cases per 1,000 pd reduced by factor 0.51 (95% CI: 0.27–0.88) (p=0.02). |
| Conterno [13];<br>ca 2%;<br>2000–5;<br>Canada;<br>ICU;<br>Medical/surgical ward;<br>CS (interrupted time series). | 1.6 d / 3.8 d | Intervention: admission screening of high-risk patients (nose, rectum, skin lesions, catheter exit sites) using PCR-based test;<br>Control: admission screening of high-risk patients using culture-based test. | Private rooms, gloves, gowns;<br>discontinued if PCR not confirmed by culture | C/I | Insignificant decrease of 0.14 nosocomial (detected >48 h after admission) MRSA cases/1,000 pd per month (95% CI: 0.18–0.46) after the introduction of PCR detection (p=0.39). |
| Cunningham [14];<br>7.0%;<br>2005–06;<br>Unired Kingdom;<br>MSICU;<br>CS (before-and-after). | <1 d / 3 d | Intervention: PCR-based nasal screening of all patients at admission and discharge;<br>Control: screening with conventional cultures of all patients at admission. | Private room (if available), standard infection control precautions, decolonisation | A | Incidence of MRSA transmission 13.89 vs 4.9/1,000 pd during culture and PCR-phase<br>(RR reduction: 0.65; 95% CI: 0.28– 1.07). |
| Harbarth [16];<br>6.7%;<br>2003–05;<br>Switzerland;<br>MSICU;<br>CS (before-and-after). | 22 h / 93 h | Phase 1: screening (nose, perineum) of high-risk patients (culture-based);<br>phase 2: universal screening (PCR-based) of all patients;<br>phase 3: same as phase 2 but general pre-emptive isolation. | Gowns, gloves, masks, decolonisation | I | Reduction in medical ICU-acquired MRSA infections (RR: 0.3; 95% CI: 0.1–0.7); no effect in surgical ICU<br>(RR: 1.0; 95% CI: 0.6–1.7). |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/ SSI=wound infections/surgical-site infections.

**Table 1G**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study;<br>MRSA[a];<br>Time;<br>Country;<br>Setting;<br>Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| PCR-based tests | | | | | |
| Harbarth [17];<br>5.1%;<br>2004–06;<br>Switzerland;<br>Surgical wards;<br>Prospective cohort study. | 22.5 h | Intervention: nasal PCR-based screening of all patients admitted to intervention wards;<br>Control: phase without any or with non-compulsory screening (switch of intervention and control wards after 9 months). | Private rooms (if available), gowns, gloves, masks, decolonisation | A, I, W/SSI | Intervention vs control phase: nosocomial (>48 h after admission) MRSA infection rate 1.11 vs 0.91/1,000 pd (adjusted incidence rate ratio: 1.20; 95% CI: 0.85–1.69); acquisition rate 1.69 vs 1.59/1,000 pd (incidence rate ratio: 1.1; 95% CI: 0.8–1.4); MRSA SSI rate 1.14 vs 0.99/100 surgical interventions (incidence rate ratio: 1.2; 95% CI: 0.8–1.7). |
| Hardy [18];<br>3.6%;<br>2005–07;<br>United Kingdom;<br>Surgical wards;<br>Prospective cohort study. | 0.9 d / 3.3 d | Intervention: Nasal PCR-based screening of all patients admitted to wards assigned to intervention group;<br>Control: control wards with culture-based screening;<br>switch of wards in intervention and control groups after 8-month period. | Private rooms, gowns, gloves, decolonisation | A | Rapid screening reduced MRSA acquisition by 1.49 times (95% CI: 1.115–2.003; p=0.007). |
| Jeyarathnam [23];<br>6.7%;<br>2006–07;<br>United Kingdom;<br>Medical/surgical ward;<br>RCT. | 22 h / 46 h | Intervention: all patients at 10 wards randomised to perform rapid or conventional screening (nose, axilla, groin, skin breaks) at admission and discharge;<br>after a 'washout' period the wards swabbed the screening methods;<br>Control: patients screened using conventional cultures. | Private rooms, gowns, gloves, decolonisation | A | No change in adjusted acquisition rate (adjusted OR: 0.91, 95% CI: 0.61–1.34; p=0.63); MRSA wound infections in the control arm vs the rapid-test arm (OR: 0.91; 95% CI: 0.48–1.7; p=0.77). |
| Jog [24];<br>2.5%;<br>2004–06;<br>United Kingdom;<br>Cardiac surgery;<br>CS (before-and-after). | NA | Intervention: nasal screening of patients admitted for cardiac surgery;<br>Control: phase without any or with non-compulsory screening. | Private rooms, standard precautions, decolonisation | W/SSI | Overall SSI rate (all organisms) 3.3% in control vs 2.2% in intervention phase; significant reduction of MRSA SSIs (1.15% vs 0.26%; p<0.05; RR: 0.77; 95% CI: 0.056–0.95). |
| Kjoonegaard [41];<br>11.6%;<br>2009–10;<br>United States;<br>MICU/SICU;<br>CS (before-and-after). | NA | Intervention: nasal (and initially perineal) screening of all ICU patients at admission;<br>Control: phase without any or with non-compulsory screening. | Contact precautions | I | Increase of healthcare-associated MRSA infections after introduction of screening (0.8/1,000 admissions vs 1.6/1,000 admissions; p=0.037). |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

**Table 1h**

Studies on the effectiveness of the use of active surveillance (screening) for meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=41)

| Study; MRSA[a]; Time; Country; Setting; Study type. | Turnaround time (PCR/ culture)[b] | Design | Screening followed by | Outcome[c] | Result |
|---|---|---|---|---|---|
| PCR-based tests | | | | | |
| Kurup [22]; 13%; 2007–08; Singapore; MSICU; CS (before-and-after). | NA | Intervention: nasal screening of all patients at admission to the ICU, weekly thereafter and at discharge; Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves, decolonisation | I | No statistically significant difference in MRSA infection rate in both ICUs combined (2.7 to 2.4/1,000 pd; p=0.48). |
| Leonhardt [25]; 1.8–4%; 2009–10; United States; Hospital-wide; CS (before-and-after). | 24 h in 90% of all cases | Intervention: nasal screening of all adult patients at admission or before in one intervention hospital; Control: phase with targeted screening of high-risk patients. | Private rooms, gowns, gloves, mask, decolonisation | I | Non-significant decline in hospital-acquired MRSA infections of 0.12 percentage points (p=0.34) during the intervention period. |
| Martinez-Capolino [26]; 13–23%; 2007–8; United States; MSICU; CS (before-and-after). | <24 h / ca 18–28 h | Intervention: nasal screening of all patients at admission and weekly thereafter; Control: phase without any or with non-compulsory screening. | Private rooms, gowns, gloves | I, B | Decrease in MRSA ventilator-associated pneumonia from 0.95 to 0.17/1,000 pd and 0.47 to 0.0/1,000 pd in Hospital 1 and 2, respectively; decrease of MRSA bloodstream infections from 0.22 to 0.13/1,00 pd and 0.93 to 0.31/1,000 pd in Hospital 1 and 2, respectively; decrease of overall hospital-wide MRSA infections only in Hospital 2 (0.63 vs 0.31/1,000 pd); statistical analysis NA. |
| Parvez [39]; 10.8%; 2008; United States; Hospital-wide; CS (before-and-after). | NA | Intervention: nasal screening of all patients at admission; Control: phase without any or with non-compulsory screening. | Contact isolation | W/SSI | No change in the MRSA SSI rate (22/3,862 (0.56%) vs 30/4,076 (0.73%); p=0.362). |
| Robicsek [29]; 6.3–8.3%; 2003–07; United States; MSICU; CS (before-and-after). | Phase 2: ca 2.5 d (in-house PCR); phase 3: 0.67 d (commercial PCR) | Intervention: nasal screening of all patients in the ICU (phase 2) and general hospital-wide screening and retesting upon ICU admission (phase 3); Control: patients without screening in phase 1. | Private rooms, gowns, gloves, decolonisation | I | Aggregate hospital-associated MRSA disease prevalence density changed by -36.2% (95% CI: -65.4% to 9.8%; p=0.17) from baseline to phase 2, and by -69.6% (95% CI: -89.2% to -19.6%; p=0.03) from baseline to phase 3. |

CI: confidence interval; CS: comparative study; ICU: intensive care unit; MICU: medical ICU; MRSA: meticillin-resistant *Staphylococcus aureus*; MSICU: medical/surgical ICU; NA: not available; OR: odds ratio; PICU: paediatric ICU; pd: patient-days; RCT: randomised controlled trial; RR: relative risk; SICU: surgical ICU; SSI: surgical-site infections;

[a] MRSA prevalence in the study setting per 100 patients admitted (except stated differently).

[b] Turnaround time of the screening test result (stratified by PCR-based test vs culture-based test, if both were compared in the respective study).

[c] Outome measures: A=MRSA acquisition/transmission; B=MRSA bacteraemia; C/I=cases of colonisation or (all/unspecified types of) infection; I=cases of several or unspecified types of infection; W/SSI=wound infections/surgical-site infections.

reviews (the literature lists of the reviews were manually screened for additional relevant publications).

Data were extracted by AWF and RK independently using a standardised form. The study designs were assigned according to a modified study design scheme published by the Centre for Reviews and Dissemination at the University of York, United Kingdom, in the NHS economic evaluation database handbook from 2007. Formal assessment of the quality of studies was not performed. Due to the different study outcomes included, formal meta-analysis was considered inappropriate. Heterogeneity in methodology and outcome measures also prevented quantitative assessment of publication bias.

## Results

The literature search identified 9,340 articles, 151 of which were retrieved as full texts after review of titles and abstracts. Of these, 69 articles fulfilled the criteria for inclusion and a further 14 articles were added after search through the literature lists of excluded review articles (Figure). Overall, 83 articles were included in the review [7-89].

## Screening

We identified 41 studies that investigated the question whether screening for MRSA carriers before or on admission had an impact on MRSA acquisition or infection rates (Table 1) [7-47].

### Culture-based screening

Twenty-five studies used culture-based screening approaches, including two randomised controlled trials (RCTs) and 23 comparative studies mostly using a before-and-after design [9,10,12,15,19-21,27,28,30-38,40,42-47]. Of these 25 studies, seven used unspecified culture-based techniques [12,21,27,28,37,40,46], eight used MRSA chromogenic media (at least partially) [19,31-34,38,45,47] and the others used mannitol salt, oxacillin salt or blood agars. An estimate for the turnaround times (TAT) of screening results was only reported in eight of the 25 studies (1 d–5.2 d) [10,12,19-21,33,34,38]. Overall, 19 of the 23 comparative studies included reported trends of decreasing rates of MRSA infection or colonisation [10,12,15,19,21,27,28,30-32,35-38,40,42,43,45,46], two reported ambiguous results [44,47], and two reported no reduction of MRSA infections or transmission [33,34]. The two RCTs found no reduction of MRSA infections or transmission [9,20].

### PCR-based screening

Sixteen studies used PCR-based screening techniques in their intervention phases, including one RCT, two prospective cohort studies and 13 comparative studies [7,8,11,13,14,16-18,22-26,29,39,41]. The TAT of the PCR screening result was reported in 11 of 16 studies (0.67 d–1.5 d) [7,11,13,14,16-18,23,25,26,29]. Overall, seven of 16 studies documented positive effects on the occurrence of MRSA infections or transmissions after implementation of screening [8,11,14,18,24,26,29]. One study reported ambiguous results [16]. Among the studies reporting a decrease of infection or transmission, five compared the intervention group (PCR-based screening) to a control group without active surveillance, with non-compulsory active surveillance or with screening of limited risk groups [8,11,24,26,29], and two compared with a control group where routine culture-based screening was performed [14,18]. Among the eight studies which could not document decreasing trends in MRSA infections or transmission following the implementation of screening, three compared PCR-based screening with culture-based screening [7,13,23], four compared the intervention to control periods without any active surveillance of MRSA [17,22,39,41], and one compared the intervention with a baseline period where PCR-based screening of selected risk patients was performed [25].

### Screening (PCR-based and culture-based) vs no screening stratified by outcome measure

In eight of nine studies (89%) using this outcome parameter, MRSA bacteraemia rates decreased after implementation of screening [8,11,21,26,28,31,32,38,47]. Incidence of MRSA acquisition or transmission decreased in three of eight studies (38%) assessing this outcome parameter [8,9,17,32-34,43,44]. Three of five studies (60%) using wound infection and surgical-site infections (SSI) as an outcome parameter showed decreasing SSI rates after implementation of screening [8,17,24,37,39]. A decrease of MRSA was observed in 20 of 23 studies (87%) using all or unspecified MRSA infections or cases of colonisation/infection as their outcome parameters [8-10,12,15-17,19,20,22,25-27,29,30,35,36,40-42,45-47]; among these studies, one found a decrease only in medical ICUs [16].

### PCR-based vs culture-based screening

Five investigations compared PCR-based to culture-based screening [7,13,14,18,23]. All five documented that the TAT was reduced when compared to culture-based approaches (Table 1). However, three studies found no difference in MRSA acquisition or infection rates [7,13,23]. In contrast, one before-and-after study found a reduction in the incidence of MRSA transmission after introduction of the PCR-based test which almost reached statistical significance, and one cohort study reported a reduction in MRSA acquisition rates [14,18].

## Decolonisation

A total of 11 RCTs, 23 comparative studies and one prospective cohort study evaluated the effectiveness of mupirocin-based nasal decontamination regimens for the prevention of *S. aureus* infections (Table 2) [48-82]. Of all 11 RCTs, six demonstrated significantly decreasing infection trends after implementation of decolonisation [48,51,52,72,73,75]; for one of these, this was only observed when selective digestive decontamination was added to nasal decolonisation [52], and for one RCT, the effect was only analysed for Gram-positive infections (which were mostly MRSA) [75]. Stratified by

types on infections prevented, the RCTs showed that decolonisation decreased deep *S. aureus* SSI [48], overall *S. aureus* infections [48,51,73], overall infection rates [52], Gram-positive pneumonia [75] and *S. aureus* exit-site infections [72].

Among the 24 non-randomised studies identified, 19 reported evidence that the use of mupirocin was effective in reducing infection. Of the seven studies performed in ICUs, six (86%) demonstrated an effect; specifically, a decrease in pneumonia and hospital-acquired *S. aureus* infection [59], in the overall infection rates in ICUs [50,70], in MRSA SSI and bloodstream infections (BSI) in ICUs [55], and in the overall number of MRSA infections in ICUs [80,81]. Non-controlled studies implementing decolonisation in non-ICU settings led to a decrease in overall and peristomal MRSA infections [57,76], in the incidence of S.aureus/MRSA SSI in surgical units [55,58,64,65,71,77,79], in overall *S. aureus*/MRSA infections in gastrointestinal surgery and orthopaedics [49,82], and in the total rate of SSI or wound infections [53,60,67].

Stratified by different implementation settings, four of five studies documented success among patients undergoing cardiothoracic surgery [53,65,66,71,77], four of six in orthopaedic departments [49,60,61,63,64,79], and six of seven in other or mixed surgical departments [54,55,58,67,73,75,82]. Moreover, seven of eight studies performed in ICU settings [50,52,55,59,68,70,80,81], two of two performed in haemodialysis units [51,72], two of five performed in different non-surgical departments [56,57,69,76,78], and one of three studies performed hospital-wide or in both medical and surgical departments [48,62,74], demonstrated successful effects of mupirocin-treatment.

Stratified by different causative organisms, eight studies showed that mupirocin-treatment led to a decrease in the overall incidence of infections due to all organisms [49,53,60,64,65,67,70,77]. In the same studies, this effect was partially non-significant for *S. aureus*/MRSA infections in particular [53,60,67,70]. Four studies reported a decrease in infections caused by methicillin-sensitive *S. aureus* (MSSA) [48,51,55,65]. Twelve investigations revealed a reduction in MRSA infections [49,50,55,57,58,64,76,77,79-82], six showed decreasing trends for *S. aureus* (MRSA and/or MSSA) infections [50,59,71-73,82] and one reported reduction of pneumonia caused by Gram-positive bacteria (mostly MRSA) [75].

Many of the studies identified in this review used mupirocin-only regimens [51,55,59,60,63,67,70-73,75,78,82]. Others combined nasal mupirocin with other topical agents to support decolonisation, including chlorhexidine [48,50,53,56-58,61,62,64-68,74,81], triclosan [49,76,79], extra-nasal use of mupirocin [69,77,80], selective digestive decontamination [52], povidone-iodine [49], and systemic antibiotics [54].

## Isolation

Focusing on the physical isolation of patients in separate single or cohort rooms, we identified one cohort study and seven comparative studies reporting on the effectiveness of this measure (Table 3) [16,83-89]. Five studies were performed in ICU settings [16,83-85,88], one in a vascular surgery ward, one in a diabetic food unit, and one hospital-wide [86,87,89]. In two of these studies, nurse cohorting was performed in addition to single-room isolation [83,86]. Overall, one cohort and three comparative studies reported on beneficial effects of single-room isolation (not performed pre-emptively) on MRSA colonisation or infection [85,86,88] and on acquisition rates [84]. Two comparative studies did not find a reduction of transmission [83] or MRSA prevalence [87].

Three studies assessed the role of pre-emptive isolation measures pending the results of screening [16,86,89]. In one before-and-after study, pre-emptive isolation precautions led to a reduction of the MRSA acquisition rate (0.21% vs 0.07%; p=0.04) [89]. In a retrospective comparative study placing all admitted patients in pre-emptive isolation, the number of nosocomial MRSA isolates was reduced (p=0.005). However, simultaneous introduction of a cohort isolation facility with dedicated staff makes the effects of this measure indistinguishable from the effects of pre-emptive isolation [86]. The third was a study that evaluated the effects of simultaneous implementation of pre-emptive isolation and a rapid screening test on the incidence of MRSA infections in two ICUs [16] resulting in a significant reduction of ICU-acquired infections in a medical but not in a surgical ICU.

# Discussion

Improving the rational use of antibiotics and the implementation of hand hygiene are clearly cornerstones of MRSA prevention and control [90-92]. Moreover, benchmarking and public reporting systems have recently been demonstrated to successfully support infection control measures [93]. However, the effectiveness of screening, decolonisation and isolation for MRSA prevention when implemented routinely in settings with endemic MRSA, remains controversial. For example, it is debated to what extent microbiological, strain-specific factors have contributed to the decreasing MRSA trends [94,95]. Therefore, the present review aimed to focus on three important measures and to summarise the current evidence for their impact on MRSA prevention.

## Screening

The strategy of screening is based on the finding that microbiological cultures performed for clinical reasons fail to detect previously unknown MRSA carriers at admission in 69 to 85% of patients [96,97]. Technically, screening can be performed by culture-based methods (screening swab streaked onto non-selective or chromogenic media) or PCR-based tests.

**TABLE 2A**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Bode [48]; 2005–07; Netherlands; Surgery and internal medicine; Randomised placebo-controlled trial. | Mupirocin 2xd and chlorhexidine gluconate (40 mg/mL) soap for 5 days; further courses of same treatment for patients staying >3 weeks. | *S. aureus* carriers only | NA | NA | NA | ↓ | Reduction of hospital-acquired MSSA infection (3.4% vs 7.7%; RR: 0.42; 95% CI: 0.23–0.75), deep MSSA SSI (RR: 0.21; 95% CI: 0.07–0.62) but not of superficial MSSA SSI 0.45 (0.18–1.11) and MSSA lower respiratory infections 0.82 (RR: 0.82; 95% CI: 0.12–5.78). | Diverse, SSI, VAP/LRTI, (BSI, UTI assessed, but small numbers) |
| Boelaert [51]; NA; Belgium; Haemodialysis; Randomised placebo-controlled trial. | Mupirocin 3xd for 2 weeks; subsequently 3x per week for 9 months. | *S. aureus* carriers only | NA | NA | NA | ↓ | Reduction of MSSA infections (1/104 patient-months vs 6/147 patient-months; p<0.05). | Diverse |
| Camus [52]; 1996–08; France; MICU; Randomised placebo-controlled trial. | Group 1: mupirocin 3xd for 5 days; again 5 days if nasal *S. aureus*; chlorhexidine gluconate (4%) total-body washing 2xd (until 24 h after extubation; max 90 days); Group 2: same as group 1 plus selective digestive decontamination | All patients irrespective of carriage | ↓[b] | NA | NA | NA | Group 1: number of acquired infections did not differ (OR: 0.98; 95% CI: 0.6– 1.58; p=0.92). Group 2: number of acquired infections incl. VAP, UTI, catheter-related infections differed (OR: 0.42; 95% CI: 0.25–0.73; p=0.002). | Diverse, VAP, UTI, BSI |
| Cimochowski [53]; 1995–99; United States; Cardiothoracic surgery; Prospective comparative study with control (before-and-after). | Mupirocin the night and morning before surgery, before surgery, then 2xd for 5 days; chlorhexidine shower before surgery. | All patients irrespective of carriage | ↓ | n.s | NA | NA | Reduction of overall SSI (0.9 vs 2.7%; p=0.005), but not *S. aureus* SSI (4/854 vs 11/992; p>0.05). | Sternal SSI |
| Cordova [54]; NA; United States; Dermatology (Mohs surgery); Retrospective comparative study with control (before-and-after). | Mupirocin 2xd for 5–7 days and oral trimethoprim-sulfamethoxazole for 5–7 days | Only MRSA carriers | NA | NA | NS | NA | MRSA SSI: 0.3% in historical cohort (12/3,633) vs 0% in treatment group (0/962); statistical analysis NA; Fisher's exact test performed by the authors of this review: p=0.08). | SSI |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

**TABLE 2B**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Dupeyron [56]; 1999–2001; France; Digestive disease unit; Prospective comparative study with control (before-and-after). | Mupirocin 3xd for 5 days; chlorhexidine (4%) every second day during mupirocin treatment; further treatment courses in case of failure. | Only MRSA carriers | NA | NA | NS | NA | Overall MRSA infections: 1.41/1,000 pd in control period and 1.46/1,000 pd in intervention period (statistical analysis NA). | Diverse |
| Dupeyron [57]; 2000–04; France; Gastroenterology; Prospective comparative study with control (interrupted-time-series). | Mupirocin 3xd for 5 days; chlorhexidine (4%) every second day during mupirocin treatment; further courses in case of failure. | Only MRSA carriers | NA | NA | ↓ | NA | Reduction of overall MRSA infections (1.41/1,000 pd in the year before intervention to 1.40, 0.74, 0.59/1,000 pd in different periods thereafter, p=0.002). | Diverse |
| Fraser [59]; 2006–07; United States; MICU; Retrospective comparative study with control (before-and-after). | Mupirocin (5 doses) | *S. aureus* carriers only | NA | ↓ | NA | NA | Reduction of *S. aureus* VAP (p=0.03; RR 0.12; 95% CI: 0.01–0.83), overall *S. aureus* infections (p=0.03; RR 0.37; 95% CI: 0.14–0.90), but NS effect on *S. aureus* BSI (p=0.28). | Diverse, BSI, VAP/LRTI |
| Gernaat-van der Sluis [60]; 1992–06; The Netherlands; Orthopaedic wards; Prospective comparative study with control (before-and-after). | Mupirocin thrice before surgery | All patients irrespective of carriage | ↓ | NS | NA | NA | Reduction of overall SSI (p=0.02), but NS reduction of *S. aureus* SSI (p=0.3). | SSI |
| Hadley [61]; 2007–09; United States; Orthopaedic wards; Retrospective comparative study with control (before-and-after). | Mupirocin (2%) for 5 days (dose unspecified); chlorhexidine once preoperatively. | All patients irrespective of carriage | NS | NA | NS | NA | No reduction of SSI rate (1.28% in the treatment vs 1.45% in the control group; p=0.809) and no reduction of MRSA SSI (0.24% vs 0.30%; NS). | SSI |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

## Table 2c

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Harbarth [62]; 1995–07; Switzerland; Hospital-wide; Randomised placebo-controlled trial. | Mupirocin 2xd for 5 days; chlorhexidine for 5 days. | Only MRSA carriers | NA | NA | NS | NA | No reduction of overall MRSA infections (3/48 vs 7/50; p=0.32). | Diverse |
| Huang [80]; 2003–06; Taiwan; Neonatal ICU; Prospective comparative study (before-and after). | Mupirocin 2xd for 5 days | Only MRSA carriers | NA | NA | ↓ | NA | Reduction of overall MRSA infections in the group of neonates treated (92/783 vs 5/450; OR: 11.85; 95% CI: 4.6-33.3). | Diverse |
| Kalmeijer [63]; 1997–09; The Netherlands; Orthopaedic wards; Randomised placebo-controlled trial. | Mupirocin 2xd until day of surgery (at least 2 doses before surgery). | All patients irrespective of carriage | NA | NS | NA | NA | No significant reduction of endogenous *S. aureus* SSI (0.3% in treatment vs 1.7% control group; RR: 0.19; 95% CI: 0.02-1.62). | SSI |
| Keshtgar [55]; 2000–06; United Kingdom; ICU and surgery; Prospective comparative study (before-and after). | Mupirocin 3xd for 5 days; chlorhexidine (use unspecified except for hairwash on days 1, 3, 5). | Only MRSA carriers | NA | NA | ↓ | ↓↑ | Reduction of MRSA BSI by 38.5% (p<0.001), MSSA BSI by 30.4% (p<0.001), MRSA SSI by 12.7% (p=0.021); but increase of MSSA SSI by 12.7% (p=0.006). | BSI, SSI |
| Kim [64]; 2005–07; United States; Orthopaedic wards; Prospective comparative study with control (before-and-after). | Mupirocin 2xd for 5 days; chlorhexidine 1xd for 5 days (3 days for MSSA). | *S. aureus* carriers only | ↓ | NA | ↓ | NS | Reduction of overall SSI (p=0.0093), MRSA SSI (0.19% vs 0.06%, p=0.0315), MSSA SSI (0.26% vs 0.13%, p=0.0937). | SSI |
| Kluytmans [65]; 1989–92; The Netherlands; Cardiothoracic surgery; Retrospective comparative study with control (before-and-after). | Mupirocin 2xd for 5 days; chlorhexidine before surgery. | All patients irrespective of carriage | ↓ | NA | NA | ↓[c] | Reduction of the overall rate of SSI (7.3% vs 2.8%; p<0.001) and of *S. aureus*/coagulase-negative staphylococcal SSI (p=0.0032). | SSI |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

**TABLE 2D**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Konvalinka [66]; 1997–2003; Canada; Cardiothoracic surgery; Randomised placebo-controlled trial. | Mupirocin 2xd for 7 days before surgery for *S. aureus* carriers only; standard pre-operative clinical practice for all patients included chlorhexidine 12 h before surgery. | *S. aureus* carriers only | NS | NS | NA | NA | No reduction of overall SSI (1.6% vs 2.4%; p=0.672) and *S. aureus* SSI (0% vs 1.6%; p=0.243). | SSI |
| Lipke [67]; 2005–07; United States; Surgery; Retrospective comparative study with control (before-and-after). | Mupirocin 2xd for 5 days; all patients: chlorhexidine morning before surgery. | Only MRSA carriers | ↓ | NA | NS | NA | Reduction of overall SSI (7/1,094 to 7/1,225; p=0.0196), but NS for MRSA SSI (8/1,094 vs 2/1,225; p=0.0538). | SSI |
| Milstone [68]; 2002–09; United States; Neonatal ICU; Retrospective comparative study with control (before-and-after). | Mupirocin for infants >36 weeks of gestational age or >4 weeks of chronological age with MRSA carriage; chlorhexidine; duration of therapy: unspecified. | Only MRSA carriers | NA | NA | NS | NA | No reduction of overall MRSA infections (95% CI: 0.002–1.03). | Diverse |
| Mody [69]; NA; United States; Long-term care facility; Randomised placebo-controlled trial. | Mupirocin 2xd for 14 days; mupirocin treatment of wounds. | *S. aureus* carriers only | NA | NS | NA | NA | No significant reduction of overall *S. aureus* infections (3/55 vs 7/47; p=0.1). | Diverse |
| Muller [70]; 1999–2003; France; MICU; Retrospective comparative study with control (before-and-after). | Mupirocin for 5 days (dose unspecified) | Only MRSA carriers | ↓ | NA | NS | NA | Reduction of overall infections (1/9 infections vs. 11/17; p=0.006), but NS for overall MRSA infections (p=0.24). | Diverse |
| Nicholson [71]; 2002–04; United States; Cardiothoracic surgery; Prospective comparative study with control (before-and-after). | Mupirocin 2xd for 7 days (if *S. aureus* carriage was confirmed) or less than 7 days (if screening was negative). | All patients irrespective of carriage | NA | ↓ | NA | NA | Reduction of *S. aureus* SSI rate (1.68% to 0.37%; p=0.006) and reduction of deep sternal *S. aureus* infections (p=0.0087). | SSI |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

**Table 2e**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Perl [73]; 1995–08; United States; Surgery; Randomised placebo-controlled trial. | Mupirocin 2xd for 5 days before surgery | All patients irrespective of carriage | NS | ↓ | NA | NA | Reduction of nosocomial *S. aureus* infection among *S. aureus* carriers (4% vs 7.7%; p=0.02); no reduction of *S. aureus* SSIs. | Diverse, SSI |
| Pofahl [58]; 2004–07; Unites States; Surgery; Retrospective comparative study (before-and after). | Mupirocin 2xd for 5 days; chlorhexidine (4%) days 1, 3, 5. | Only MRSA carriers | NA | NA | ↓ | NA | Reduction of MRSA SSI (0.23% vs 0.09%); pronounced in joint-replacement surgery (0.30– 0%; p=0.04). | SSI |
| Ridenour [81]; 2003–04; United States; MICU; Retrospective comparative study (before-and after). | Mupirocin 2xd for 5 days; chlorhexidine 1xd for 7 days. | Only MRSA carriers | NA | NA | ↓ | NA | Reduction of MRSA incidence density of colonisation or infection (8.45 vs 4.05/1,000 pd; p=0.048). | Diverse |
| Robicsek [74]; 2006–07; United States; Hospital-wide; Prospective cohort study. | Mupirocin 2xd for 5 days and chlorhexidine (4%) days 1, 3, 5 | Only MRSA carriers | NA | NA | NS | NA | No reduction of overall MRSA infections (NS); trend towards delayed infections in treatment group (15.5 days vs 50 days until infection; p=0.06). | Diverse |
| Sandri [50]; 1999–2003; Brazil; General ICU; Prospective comparative study without control group. | Mupirocin 3xd for 5 days and chlorhexidine 1xd for 3 days | Only MRSA carriers | NA | ↓ | ↓ | NA | Reduction of nosocomial *S. aureus* infections (9.9% vs 3.3%; p=0.001) and MRSA infections (8.2% vs 2.8%; p=0.001). | Diverse |
| Sankar [49]; 2000–01; United Kingdom; Orthopaedic wards; Prospective comparative study (before-and after). | Mupirocin or povidone iodine or triclosan (unspecified treatment) | Only MRSA carriers | ↓ | NA | ↓ | NA | Reduction of overall hospital-acquired infections (8.5% vs 3.5%; p<0.05) and overall MRSA infections (p<0.05). | Diverse |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

**TABLE 2F**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Suzuki [75]; 1998–2000; Japan; Abdominal digestive surgery; Randomised controlled trial. | Mupirocin 3xd for 3 days before the operation | All patients irrespective of carriage | NS | NA | ↓[d] | NA | No reduction of overall infections (mostly caused by Gram-negative bacteria); reduction of VAP due to Gram-positive bacteria (mostly MRSA) (p=0.028). | Diverse, VAP/ LRTI, SSI |
| The Mupirocin Study Group [72]; NA; Europe; Haemodialysis; Randomised placebo-controlled trial. | Mupirocin 2xd for 5 consecutive days every 4 weeks | *S. aureus* carriers only | NS | ↓ | NA | NA | Reduction of *S. aureus* exit-site infections (p=0.006); no reduction of overall exit-site infections (p=0.17), tunnel infections and peritonitis (NS). | Exit-site infections |
| Thomas [76]; 2002–06; United Kingdom; Gastroenterology; Prospective comparative study with control (before-and-after). | Mupirocin 3xd and daily 2% triclosan for 5 days | Only MRSA carriers | NA | NA | ↓ | NA | Reduction of peristomal MRSA infections (5/42–7/24 vs 1/47, p<0.01). | Peristomal infections |
| Walsh [77]; 2004-10; United States; Cardiothoracic surgery; Prospective comparative study with control (before-and-after). | Mupirocin (dose unspecified) for 5 days; sterile gauze coated with mupirocin on exit site. | All patients irrespective of carriage | ↓ | NA | ↓ | NS | Reduction of overall wound infections (p<0.01); 93% reduction of MRSA SSIs (32/2,766 vs 2/2,496; p<0.001); MSSA SSI rate NS (5/2,766 vs 2/2,496; p=0.27). | SSI |
| Wertheim [78]; 1999–2001; The Netherlands; Non-surgical departments; Randomised placebo-controlled trial. | Mupirocin 2xd for 5 days | *S. aureus* carriers only | NS | NA | NA | NS | No reduction of overall nosocomial *S. aureus* infections (2.6% vs. 2.8%, risk difference 0.2 percentage points; 95%CI: -1.5-1.9). Trend towards delayed time of infection onset (12 days vs 25 days; p=0.28). | Diverse |
| Wilcox [79]; 1999–2000; United Kingdom; Orthopaedic wards; Prospective comparative study with control (before-and-after). | Mupirocin for 5 days (dose unspecified), starting one day before surgery and ending 4 days after surgery; triclosan 2% on the day before surgery. | All patients irrespective of carriage | NS | NA | ↓ | NS | Reduction of MRSA SSI (23/1,000 operations vs 3.3/1,000 operations; p<0.001); no reduction of overall SSI rate and MSSA SSI rate (NS). | SSI |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

**Table 2G**

Studies on the effectiveness of *Staphylococcus aureus* decolonisation using mupirocin-based regimens, published 2000–2012 (n=35)

| Study; Time; Country; Setting; Study type. | Treatment regimen[a] | Treatment of | Effects of treatment stratified by pathogen | | | | Effect of treatment | Types of infections analysed separately |
|---|---|---|---|---|---|---|---|---|
| | | | All organisms | MRSA+ MSSA | MRSA | MSSA | | |
| Yano [82]; 1996–08; Japan; Gastrointestinal surgery; Prospective comparative study with control (before-and-after). | Mupirocin 3xd for 3 days preoperatively | All patients irrespective of carriage | NS | ↓ | ↓ | NS | Reduction of MRSA infections after upper gastrointestinal surgery (9/128 vs 0%; p=0.001); NS for MSSA infections (p=0.056). | Diverse |

BSI: bloodstream infections; CI: confidence interval; diverse: diverse or all types of infections ICU: intensive care unit; LRTI: lower respiratory tract infections; MICU: medical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; MSSA: meticillin-sensitive *Staphylococcus aureus*; NA: no data available; NS: not significant; ↓ reduction; ↑ increase; OR: odds ratio; pd: patient-days; RR: relative risk; SSI: wound infections or surgical-site infection, VAP: ventilator-associated pneumonia; UTI: urinary tract infections;

[a] Mupirocin refers to mupirocin nasal ointment unless specified otherwise. Chlorhexidine and triclocan body washes, 1xd or 2xd or 3xd refers to application 1x, 2x or 3x per day.

[b] Only when selective digestive decontamination was added to mupirocin-treatment.

[c] MSSA and coagulase-negative staphylococci.

[d] Gram-positive infections (mostly MRSA).

### Screening vs no screening

Of 36 cohort and comparative studies investigating the effectiveness of compulsory screening compared with no or non-compulsory screening, 27 reported decreasing trends in the rates of MRSA infection or acquisition; this is in accordance with a meta-analysis describing a decrease in MRSA bloodstream infections (relative risk (RR): 0.54; 95% CI: 0.41–0.71) and surgical site infections (RR: 0.69; 95% CI: 0.46–1.01) [98]. On the other hand, two RCTs found that MRSA acquisition or infection in the intervention groups did not differ significantly from the control groups [9,20]. However, in both studies, the median time for reporting a positive screening result was very long (3 days and 5.2±1.4 days), which led to delayed implementation of contact precautions. In addition, compliance with transmission-based precautions was not as required [20] and the prevalence of MRSA infection was low in one of the studies [9]. Comparing successful and unsuccessful interventions, we did not find clear differences between the studies regarding the specimens used for screening (nasal swab only vs other swabs in addition) or the patient population included (all patients admitted vs high-risk patients only).

There was a tendency that studies including 'incidence of MRSA acquisition' as an outcome parameter, reported a success less frequently (three of eight studies) compared with studies focusing on MRSA infection rates using the outcome parameters 'occurrence of bacteraemia' (eight of nine studies) or 'SSI' (three of five studies). The reason for this effect is not known, but it could highlight that screening does not necessarily affect the rate of cross-transmission on the ward, unless it is linked to additional preventive measures; decolonisation, for instance, was not performed in two of the the studies measuring incidence of acquisition [33,34], while in two others, single-room isolation was omitted or only performed if available [9,17].

In conclusion, we found evidence that screening can help decrease MRSA infection rates in hospitals. This is also supported by macro-epidemiological data and mathematical models showing that without screening, other infection control measures might fail to effectively reduce MRSA spread [99-102]. However, the included RCTs did not confirm the findings of non-controlled studies. This makes it impossible to firmly recommend the implementation of screening in all settings. However, the evidence provided can support the introduction of a programme for active surveillance of MRSA in settings that have hyperendemic MRSA cross-infections in spite of a high level of compliance with standard precautions. Clearly, the implementation of screening needs to be linked to other targeted infection control measures (e.g. hand hygiene) to achieve optimal impact.

### Culture-based screening vs PCR-based screening

Screening for MRSA colonisation of patients at admission using culture-based approaches requires 24 to

## Table 3a

Studies on the effectiveness of isolation measures against meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=8)

| Study | MRSA | Time | Country | Specialty | Study type | Design | Outcome [a] | Result |
|---|---|---|---|---|---|---|---|---|
| Bracco [84] | 1.1% | 2002– 04 | Canada | MSICU | Prospective cohort study | Intervention: patients hosted in single rooms and bay rooms; allocation was not randomized; rates of nosocomial cross-contamination among patients hosted in single-rooms were assessed; Compared to: rates of nosocomial cross-contamination among patients hosted in bay rooms with 2–6 beds. | A | Incidence density of MRSA acquisition was 4.1/1,000 pd in bay rooms compared with 1.3/1,000 pd in single rooms (p<0.001); the RR of acquiring MRSA was 0.65 in single vs bay rooms; rates of BSI and positive catheter tips were also significantly reduced in single rooms compared to bay rooms. |
| Cepeda [83] | NA | 2000– 01 | United Kingdom | MSICU | Prospective comparative study with control (interrupted) time-series | Intervention: phase 1 and 3: MRSA patients moved to single rooms or bays; Compared to: phase 2: no move to single rooms or bays. | A | No difference regarding transmission between the move and non-move phase; 0.73 (95% CI: 0.49–1.10; p=0.94) |
| Cheng [85] | NA | 2002– 09 | China | MSICU | Retrospective comparative study with control (interrupted-time-series) | Intervention: phase 2 (2004–06): patients with MRSA detected in clinical specimens were placed in single rooms; phase 3 (2006–09) MRSA patients were cared for in single rooms and a hand hygiene campaign was introduced; Compared to: phase 1 (2002–04): patients with MRSA detected from clinical specimens were not moved to single rooms. | B, I | ICU-onset non-bacteraemic MRSA infections decreased from 3.54/1,000 pd in phase 1 to 2.26 in phase 2 (p=0.042) and 1.02 (p=0.006) in phase 3; bacteraemic MRSA infection decreased from 1.94/1,000 pd (phase 1) to 0.9 (phase 2, p=0.005) and 0.28 (phase 3, p =0.021). |
| Curran [86] | NA | 2002– 04 | United Kingdom | Vascular surgery ward | Retrospective comparative study with control (interrupted-time-series) | Intervention: opening of a cohort area for MRSA colonised or infected patients; all admissions were placed in an isolation facility and then transferred to the cohort or the non-cohort area dependent on the results of screening; Compared to: time before the cohort area was opened. | C/I | Reduction of the number of nosocomial MRSA isolates (p=0.005) after opening of the cohort area; reduction was sustained after cohort area was discontinued. |
| Fazal [87] | NA | 1991– 94 | Unites States | Hospital-wide | Retrospective comparative study with control (before-and-after) | Intervention: patients with MRSA no longer placed in private rooms plus transmission-based precautions (gloves, gowns, masks); the latter (without single room) were continued only on the ICU; Compared to: all patients with MRSA were placed in single rooms with transmission-based precautions. | C/I | Decrease of the percentage of MRSA among all *S. aureus* isolates (from 34% to 20%; p=0.001); discontinuing single room isolation did not result in an increase in the prevalence of MRSA. |
| Gregory [88] | 1.3% | 2000– 07 | United States | Neonatal ICU | Retrospective comparative study without control | Intervention: screening of all patients; in case of MRSA: isolation in a cohort plus contact precautions (gloves and gowns); Compared to: no control group; observation over time. | C/I | Incidence of MRSA decreased from 1.79/1,000 pd in 2000 to 0.15 in 2005 (yearly 31% decrease; p=0.001). However, incidence increased to 1.26/1,000 pd in 2007, accompanied by the occurrence of CA-MRSA types. |
| Harbarth [16] | 6.7% | 2003– 05 | Switzerland | MSICU | Prospective comparative study with control (before-and-after) | Phase 1: screening of high-risk patients (culture-based); phase 2: universal screening (PCR-based); phase 3: same as phase 2 but general pre-emptive isolation. | I | On-admission screening and pre-emptive isolation reduced medical ICU-acquired MRSA infections (RR: 0.3; 95% CI: 0.1–0.7), but had no effect in the surgical ICU (RR: 1.0; 95% CI: 0.6–1.7). |

BSI: bloodstream infection; CA: community-acquired; ICU: intensive care unit; MSICU medical-surgical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; pd: patient-days; RR: relative risk.

[a] Outcome measures: A=MRSA acquisition/transmission, B=MRSA bacteraemia, C/I=cases of colonisation or infection, I=cases of several or unspecified types of infection.

**Table 3B**

Studies on the effectiveness of isolation measures against meticillin-resistant *Staphylococcus aureus*, published 2000–2012 (n=8)

| Study | MRSA | Time | Country | Specialty | Study type | Design | Outcome [a] | Result |
|---|---|---|---|---|---|---|---|---|
| Lecornet [89] | 31% | 1997– 2003 | France | Diabetic foot unit | Prospective comparative study with control (before-and-after) | Intervention: pre-emptive contact isolation of all patients until the screening results were negative; Compared to: isolation precautions performed after MRSA was isolated from the screening sample. | A | The acquisition rate was 7/10,154 MRSA-free pd (0.07%) in the intervention phase vs 6/2,854 MRSA-free pd (0.21%) in the phase without pre-emptive isolation (p=0.04). The relative risk of acquiring MRSA was 0.33 (95% CI: 0.11–0.98) in the intervention vs the control phase. |

BSI: bloodstream infection; CA: community-acquired; ICU: intensive care unit; MSICU medical-surgical intensive care unit; MRSA: meticillin-resistant *Staphylococcus aureus*; pd: patient-days; RR: relative risk.

[a] Outcome measures: A=MRSA acquisition/transmission, B=MRSA bacteraemia, C/I=cases of colonisation or infection, I=cases of several or unspecified types of infection.

72 hours until the results are available on the wards [103,104]. During this time MRSA can spread among inpatients. Therefore, various PCR-based methods have been developed to reduce the TAT [105,106]. Reduction of TAT was indeed confirmed by all studies on PCR-based tests identified in this review. But these studies mostly did not find a significant reduction of MRSA infection or acquisition rates. These results are in accordance with data from a meta-analysis showing that, compared with cultures, the use of rapid tests was not associated with a significant decrease in MRSA acquisition rates (risk ratio 0.87; 95% CI: 0.61–1.24) [98]. On the other hand, we found two studies reporting on a significant reduction of MRSA acquisition and a trend towards declining transmission [14,18]. They demonstrate that implementation of PCR-based surveillance can be beneficial at least in facilities where culture results have a very long TAT (>3 days) [14,18].

We conclude that in settings where MRSA screening based on cultures, followed by the implementation of additional precautions, is already implemented, the current evidence does not suggest replacing or supplementing culture-based surveillance with rapid tests. However, besides accelerating the implementation of additional precautions, the high negative predictive value of MRSA rapid tests may also be useful when discontinuing contact precautions (including single-room isolation) in settings where they are implemented pre-emptively for suspected MRSA carriers [103]. However, the reliability of a negative nasal rapid test has not been evaluated in situations where pre-emptive isolation is performed for high-risk patients, who are often carrying MRSA at extranasal sites (e.g. wounds). Furthermore, using rapid tests in low prevalence settings may increase the number of false-positive tests (positive predictive values: 31–78%) [103,107-110].

## Decolonisation

The effectiveness of mupirocin nasal ointment to eradicate MRSA has been estimated to be 94% one week after treatment and 65% after a 14-day follow-up period [111,112]. Effectiveness of MRSA decolonisation therapy is obviously limited when extranasal sites are colonised [113]. Since nasal carriage of *S. aureus* is a major risk factor for subsequent nosocomial infection, there is a theoretical rationale that eradicating *S. aureus* from the nares can reduce the development of infection. It is, however, controversial to what extent studies assessing the effectiveness of decolonisation among patients carrying MSSA also hold lessons for MRSA [114]. In this review, we have identified only four studies in which mupirocin-treatment was not restricted to MRSA carriers and where effects on MRSA and MSSA infections were reported separately. All four documented a decrease in MRSA, but found insignificant results for MSSA [64,77,79,82]. However, this does not mean that mupirocin-based decolonisation is ineffective against MSSA in general, since two randomised trials have reported a reduction of MSSA infections [48,51]. The reasons for this discrepancy are

unknown, and the question whether results obtained for MSSA can be transferred to MRSA is unresolved. Despite potential local differences in mupirocin susceptibility and the occurrence of clonal lineages [114], a plausible biological explanation why results on MSSA decolonisation treatment should not be applied for MRSA, is currently lacking. Therefore, we have explicitly included studies dealing with *S. aureus* decolonisation. However, future studies will have to assess in detail the differences between the preventive effectiveness of MSSA and MRSA decolonisation.

Regarding the setting of implementation, we found that 14 of 18 studies carried out mostly in surgical settings have found a reduction in infection rates, whereas six of 10 studies which did not report effectiveness, were performed mostly in non-surgical settings [56,62,68,69,74,78]. However, preventive effects have been documented for non-surgical patients, e.g. in haemodialysis units, ICUs or in gastroenterology [50 ,51,55,57,59,68,70,72,76,81].

Overall, we conclude that, taking into account local rates of healthcare-associated infections and infection control conditions, mupirocin-based decolonisation therapy should be considered for selected *S. aureus* carriers who are at high risk of developing nosocomial *S. aureus* infections. The best evidence is available for patients undergoing cardiothoracic or orthopaedic surgery. Of note, the preventive use of mupirocin for decolonisation is constrained by the development of resistance, found in 1% of all subjects when mupirocin was used for short-term prophylaxis. Increasing low-level mupirocin resistance (8–256 µg/mL) has recently been reported in parallel to increased mupirocin consumption [112,115,116].

### Isolation

There are multiple approaches to organise isolation measures: Patients can be transferred to special isolation wards, housed in nursing cohorts with designated staff, isolated in single or cohort rooms on general wards without designated personnel, or housed in the same room as patients not affected by MRSA while applying barrier precautions (e.g. gloves and gowns) when caring for the MRSA patient. In this review, we focussed on single room or cohort room isolation because this measure is sometimes debated as it can be associated with disadvantages for the isolated patient [117]. Moreover, in settings with a high prevalence of MRSA, isolation of patients may be hindered due to insufficient side room capacity and financial constraints, if isolation results in bed-blocking.

Overall, we found four studies showing that single room isolation led to a reduction in nosocomial MRSA acquisition and in the incidence of MRSA infection [84-86,88]. In contrast, in a prospective interrupted-time-series study it was found that, MRSA acquisition was not different in phases during which MRSA-colonised or infected patients were moved to single or cohort isolation, compared with phases during which they were not moved [83]. However, limitations of this study are delayed notification of screening results, a high number of missed screenings (80–87% of patients at admission and 71–75% at discharge) and low compliance with hand hygiene (21% compliance) [83]. Moreover, a retrospective comparative study showed that discontinuing single-room isolation and applying transmission-based precautions (e.g. masks, gowns, gloves) for MRSA patients did not lead to an increase in the prevalence of MRSA. However, that study did not measure the occurrence of transmission on the wards and the incidence of MRSA infections [87].

We conclude that the limited evidence from non-controlled studies which is available to support the use of single-room isolation for MRSA (outside of outbreaks) should inspire further research in this field to facilitate the development of evidence-based guidance in future, also for the prevention and control of other multidrug-resistant organisms. However, the majority of studies identified and observations made during outbreaks support the use of single-rooms [3]. Therefore, where facilities (isolation wards, single rooms, cohort rooms) for the isolation of MRSA patients are available, their use should be recommended.

In all investigations identified, it is difficult to estimate to what extent the observed preventive effects were attributable to pre-emptive isolation or to other measures implemented in parallel [16,86,89]. Consequently, there is a need to assess the evidence for the use of pre-emptive isolation measures in hospitals. This is of major importance, because authors evaluating PCR-based screening tests often suggested that rapid tests could accelerate the start of isolation precautions [16,103,118]. However, these advantages cannot be assessed adequately as long as the additional value of pre-emptive isolation is unclear.

## Conclusion

We have documented that the evidence for the effectiveness of three major MRSA prevention and control measures does not allow for clear guidance offering 'one-size-fits-all' solutions, because the effectiveness of these interventions seems highly depending on the prevalence of MRSA, compliance with general infection control measures (e.g. hand hygiene), the incidence and type of infections and the transmission rates within the respective setting of implementation. This is documented by the ambiguous study results presented here. In addition, models on the effectiveness of MRSA prevention strategies in different settings have shown that even measures which are performed highly effectively in outbreaks or low-prevalence areas, failed to control MRSA when applied for long-term control or in high-prevalence settings [119]. These difficulties have led to the development of models describing the effects and costs associated with universal vs selective MRSA screening in different settings, which may facilitate the implementation of local

standards [104,120]. Moreover, some authors have recently described the effectiveness of several preventive bundles comprising the measures reviewed here in combination with other interventions. For example, it was shown that universal nasal screening, contact precautions for patients colonised or infected with MRSA, hand hygiene, and changes in the institutional culture of responsibility reduced MRSA infections by 62% [99]. Others have identified that structural factors such as engaging front-line staff, building multidisciplinary teams, providing monitoring and feedback, and acquiring management support were key measures for the success of MRSA prevention [121]. The evaluation of such bundles with respect to their effects, feasibility and applicability in different healthcare systems (e.g. different countries), clinical departments and patient collectives could in the future guide preventive efforts. Compared to assessing the effects of single preventive measures separately (as done in this review), the main advantage of assessing the effects of bundles is that they are planned specifically for targeted healthcare sectors, and the assessment can take into account the financial and other structural conditions in the respective settings.

In this review, we did not restrict the eligibility criteria to controlled studies such as RCTs, although quasi-experimental study designs are prone to be associated with various biases (e.g. selection bias or size of study population). This was done because only very few controlled investigations have been published. In addition, among the 14 RCTs included, most of which were performed for assessing the effectiveness of decolonisation therapy, a majority did either include patients affected by MSSA or did not stratify their outcomes for MSSA and MRSA infections. This makes the results, even of these formally 'high-quality' studies, disputable. Against this background, we decided not to perform a formal grading of the quality of the included studies, but rather to present the study results holistically and leave their use in various settings and countries open for interpretation.

The controversy about different implementation pathways for screening, isolation and decolonisation should not obscure the fact that the beneficial effects of MRSA control measures in general [120] support the recommendations made in many European national MRSA policies from low prevalence countries (e.g. the Nordic countries and the Netherlands) and high prevalence countries (e.g. France, Germany, and the United Kingdom), where a combination of these measures are the standard of care and a reduction in MRSA infections has recently been achieved by coordinated efforts even in high prevalence settings [5,122].

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## Conflict of interest

SH is member of the speakers' bureau for bioMérieux and Pfizer, the scientific advisory board of Destiny Pharma, DaVolterra and bioMérieux. RLS is member of the Novartis advisory board. AWF has received fees from Siemens, Boehringer Ingelheim and Bayer; RLS from Pfizer, Leo Pharma, RibXrom and The Medicines Company; BDC from Sanofi Pasteur, Pfizer, Esoform/Ecolab and Vemacare.
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## Authors' contributions

RK and AWF did the literature search and screened titles and abstracts for relevant articles. RK and AWF extracted data from the full-texts. RK, AWF, KB, BC, JEvGP, SH, JK, MM, GP, RLS, MJS, ET and WW contributed to data collection, formulating the conclusions and writing of the manuscript.

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